**Application No.:** 10/081,072

Office Action Dated: December 29, 2003

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

## 1. (Original) A compound of formula (1):

$$R^1 - X$$
 $R^2$ 
 $R^3$ 
 $R^3$ 
 $R^3$ 
 $R^3$ 
 $R^3$ 
 $R^3$ 
 $R^3$ 

wherein

 $R^1$  is a group  $Ar^1L^2Ar^2Alk$ - in which:

Ar<sup>1</sup> is an optionally substituted aromatic or heteroaromatic group;

L<sup>2</sup> is a covalent bond or a linker atom or group;

Ar<sup>2</sup> is an optionally substituted arylene or heteroarylene group;

and Alk is a chain

in which R is a carboxylic acid (-CO<sub>2</sub>H) or a derivative or biostere thereof;

X is an -O- or -S- atom or -N( $\mathbb{R}^2$ )- group in which:

 $R^2$  is a hydrogen atom or a  $C_{1-6}$ alkyl group;

V is an oxygen (O) or sulphur (S) atom;

 $R^x$ ,  $R^y$  and  $R^z$  which may be the same or different is each an atom or group  $-L^1(Alk^1)_n(R^3)_v$  in which  $L^1$  is a covalent bond or a linker atom or group,  $Alk^1$  is an optionally substituted aliphatic or heteroaliphatic chain,  $R^3$  is a hydrogen or halogen atom or group selected from  $-OR^{3a}$  [where  $R^{3a}$  is a hydrogen atom or an optionally substituted straight or branched  $C_{1-6alkyl}$  group or  $C_{3-8}$  cycloalkyl group],  $-SR^{3a}$ , -CN or an optionally substituted cycloaliphatic, heterocycloaliphatic, polycycloaliphatic, heteropolycycloaliphatic, aromatic or heteroaromatic group, n is zero or the integer 1 and v is the integer 1, 2 or 3 provided that when n is zero and  $L^1$  is a covalent bond v is the integer 1;

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or R<sup>z</sup> is an atom or group as previously defined and R<sup>x</sup> and R<sup>y</sup> are joined together to form an optionally substituted spiro linked cycloaliphatic or heterocycloaliphatic group; and the salts, solvates, hydrates and N-oxides thereof.

- 2. (Original) A compound according to claim 1 in which Alk is a  $-CH_2CH(R)$  or  $-CH(CH_2R)$  chain.
- 3. (Original) A compound according to claim 1 in which R is a carboxylic acid (-CO<sub>2</sub>H) group.
- 4. (Original) A compound according to claim 1 in which R is an esterified carboxyl group of formula -CO<sub>2</sub>Alk<sup>7</sup>.
- 5. (Original) A compound according to claim 1 in which X is an  $-N(R^2)$  group.
- 6. (Original) A compound according to claim 5 in which R<sup>2</sup> is a hydrogen atom.
- 7. (Original) A compound according to claim 1 in which Ar<sup>2</sup> is an optionally substituted phenylene group or an optionally substituted pyridinediyl group of formula:

$$a \xrightarrow{N} b$$
 or  $a \xrightarrow{N} b$ 

where a and b signify the points of attachment of L<sup>2</sup> and Alk respectively.

- 8. (Original) A compound according to claim 1 in which Ar<sup>1</sup> is an optionally substituted phenyl or five-, six- or ten-membered heteroaromatic group.
- 9. (Original) A compound according to claim 8 in which Ar<sup>1</sup> is an optionally substituted pyridyl, pyrimidinyl, naphthyridinyl, quinolinyl or isoquinolinyl group.

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- (Original) A compound according to claim 1 in which R<sup>2</sup> is a halogen atom. 10.
- 11. (Original) A compound according to claim 1 in which R<sup>2</sup> is an optionally substituted C<sub>1-8</sub>alkyl group.
- (Original) A compound according to claim 1 in which  $R^z$  is a group  $-L^1(Alk^1)_nR^3$  in 12. which  $L^1$  is an -O-, -S- or -Se- atom or -S(O)- or  $-N(R^8)$ - group.
- 13. (Original) A compound according to claim 12 in which n is zero.
- (Original) A compound according to claim 12 in which n is the integer 1 and Alk<sup>1</sup> is 14. an optionally substituted C<sub>1-6</sub>alkylene chain.
- (Original) A compound according to claim 12 in which R<sup>3</sup> is a hydrogen atom or an 15. optionally substituted C<sub>3-10</sub>cycloaliphatic, C<sub>3-10</sub>heterocycloaliphatic, C<sub>6-12</sub>aromatic or  $C_{1-9}$ heteroaromatic group.
- (Original) A compound according to claim 1 in which R<sup>2</sup> is a group -L<sup>1</sup>(Alk<sup>1</sup>)<sub>n</sub>R<sup>3</sup> in 16. which L<sup>1</sup> is a covalent bond.
- 17. (Original) A compound according to claim 16 in which n is zero.
- 18. (Original) A compound according to claim 16 in which n is the integer 1 and Alk<sup>1</sup> is an optionally substituted C<sub>1-6</sub>alkylene chain.
- (Original) A compound according to claim 16 in which R<sup>3</sup> is a hydrogen atom or an 19. optionally substituted C<sub>3-10</sub>cycloaliphatic, C<sub>3-10</sub>heterocycloaliphatic, C<sub>6-12</sub>aromatic or  $C_{1-9}$ heteroaromatic group.

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20. (Original) A compound according to claim 1 in which  $R^x$  and  $R^y$  is each an optionally substituted  $C_{1-8}$ alkyl group.

- 21. (Original) A compound according to claim 1 in which R<sup>x</sup> and R<sup>y</sup> are joined to form an optionally substituted spiro linked C<sub>3-10</sub> cycloaliphatic or C<sub>3-10</sub>heterocycloaliphatic group.
- 22. (Original) A compound which is:

(2S)-2-[(3-Oxospiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-

dichloroisonicotinoyl)amino|phenyl}propanoic acid

 $(2S) - 2 - [(3 - Oxospiro[3.5]non - 1 - en - 1 - yl)amino] - 3 - \{4 - [(3 - methyl[2,7]naphthyridin - 1 -$ 

yl)oxy]phenyl}propanoic acid

(2S)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-

dichloroisonicotinoyl)amino|phenyl}propanoic acid

(2S)-2-[(2-Bromo-4,4-dimethyl-3-oxo-1-cyclobutenyl)amino]-3-{4-[(3,5-

dichloroisonicotinoyl)amino|phenyl}propanoic acid

(2S)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{4-[(2,7)naphthyridin-1-

yloxy]phenyl}propanoic acid

 $(2S)-2-[(2-Bromo-3-oxo-7-oxaspiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-1)]}$ 

dichloroisonicotinoyl)amino|phenyl}propanoic acid

(2S)-2-{(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino}-3-(2,6-dimethoxy[1,1'-

biphenyl]-4-yl)propanoic acid

 $(2S)-2-[(3-Oxospiro[3.6]dec-1-en-1-yl)amino]3-{4-[(3,5-dichloroiso-$ 

nicotinoyl)amino]phenyl}propanoic acid

 $(2S)-2-[(2-Bromo-3-oxospiro[3.6]dec-1-en-1-yl)amino]-3-{4-[(3,5-4)]}$ 

dichloroisonicotinoyl)amino]phenyl}propanoic acid

(2S)-2-{[4,4-Dimethyl-2-(phenylselenenyl)-3-oxo-1-cyclobutenyl]amino}-3-{4-[(3,5-1)]-3-(2S)-2-{[4,4-Dimethyl-2-(phenylselenenyl)-3-oxo-1-cyclobutenyl]amino}

dichloroisonicotinoyl)amino|phenyl}

propanoic acid

(2S)-2-[(2-Bromo-7-methoxy-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-

dichloroisonicotinoyl)amino|phenyl}propanoic acid

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(2S)-2-\{(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)-2-(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]
methyl[2,7]naphthyridin-1-yl)oxy]phenyl}propanoic acid
(2S)-2-{[2-(Phenylsulfanyl)-4,4-dimethyl-3-oxo-1-cyclobutenyl]
amino}-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
(2S)-2-[(2-Chloro-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-
dichloroisonicotinoyl)amino]phenyl}propanoic acid
                           (2S)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(3-oxo-2-pyridin-3-
yl-spiro[3.5]non-1-en-1-ylamino)propanoic acid
(2S)-2-[(2-Iodo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-
dichloroisonicotinoyl)amino]phenyl}propanoic acid
(2S)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{5-[(3,5-1)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{5-[(3,5-1)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{5-[(3,5-1)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{5-[(3,5-1)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{5-[(3,5-1)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{5-[(3,5-1)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{5-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)-2-[(3,5-1)
dichloroisonicotinoyl)amino|pyridin-2-yl}propanoic acid
(2S)-2-[(2-Chloro-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{5-[(3,5-
dichloroisonicotinoyl)amino]pyridin-2-yl}propanoic acid
                          (2S)-2-[(2-Chloro-3-oxo-7-oxa-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-
dichloroisonicotinoyl)amino]phenyl}propanoic acid
(2S)-2-[(2-Chloro-3-oxo-spiro[3.6]dec-1-en-1-yl)amino]-3-{4-[(3,5-
dichloroisonicotinoyl)amino]phenyl}propanoic acid
(2S)-2-[4,4-Dimethyl-2-(1-methyl-1H-tetrazol-5-ylsulfanyl)-3-oxo-cyclobut-1-
enylamino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
(2S)-2-[(2-Bromo-3,7,7-trioxo-7\square<sup>6</sup>-thia-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-1)]-2-[(2-Bromo-3,7,7-trioxo-7\square<sup>6</sup>-thia-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-1)]-2-[(2-Bromo-3,7,7-trioxo-7\square<sup>6</sup>-thia-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-1)]-2-[(2-Bromo-3,7,7-trioxo-7\square<sup>6</sup>-thia-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-1)]-2-[(2-Bromo-3,7,7-trioxo-7\square<sup>6</sup>-thia-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-1)]-2-[(2-Bromo-3,7,7-trioxo-7\square<sup>6</sup>-thia-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-1)]-2-[(2-Bromo-3,7,7-trioxo-7\square<sup>6</sup>-thia-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-1)]-2-[(2-Bromo-3,7,7-trioxo-7\square<sup>6</sup>-thia-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-1)]-2-[(2-Bromo-3,7,7-trioxo-7]-(2-Bromo-3,7,7-trioxo-7)-[2-Bromo-3,7,7-trioxo-7]-[2-Bromo-3,7,7-trioxo-7]-[2-Bromo-3,7,7-trioxo-7]-[2-Bromo-3,7,7-trioxo-7]-[2-Bromo-3,7,7-trioxo-7]-[2-Bromo-3,7,7-trioxo-7]-[2-Bromo-3,7,7-trioxo-7]-[2-Bromo-3,7,7-trioxo-7]-[2-Bromo-3,7,7-trioxo-7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3,7]-[2-Bromo-3
dichloroisonicotinoyl)amino]phenyl}propanoic acid
(2S)-2-[(2-Chloro-3-oxo-spiro[3.4]oct-1-en-1-yl)amino]-3-{4-[(3,5-dichloro-
isonicotinoyl)amino]phenyl}propanoic acid
(2S)-2-[(2-Bromo-3-oxo-spiro[3.4]oct-1-en-1-yl)amino]-3-{4-[(3,5-
dichloroisonicotinoyl)amino]phenyl}propanoic acid
(2S)-2-[(2-Methylsulfanyl-3-oxo-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-
dichloroisonicotinoyl)amino]phenyl}propanoic acid
(2S)-2-(2-Fluoro-3-oxo-spiro[3.5]non-1-en-1-ylamino)3-{4-[(3,5-
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dichloroisonicotinoyl)amino]phenyl}propanoic acid

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- (2S)-2-[(2-Fluoro-3-oxo-7-oxa-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl} propanoic acid
- (2*S*)-2-[(4,4-Dimethyl-2-methylsulfanyl-3-oxo-cyclobut-1-enyl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2*S*)-2-[(2-Isopropylsulfanyl-4,4-dimethyl-3-oxo-cyclobut-1-enyl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(2-Isopropylsulfanyl-3-oxo-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(2-Isopropylsulfanyl-4,4-dimethyl-3-oxo-cyclobut-1-enyl)amino]-3-[4-
- ([2,7]naphthyridin-1-ylamino)phenyl]propanoic acid
- (2S)-2-[(2-Isopropylsulfanyl-3-oxo-spiro[3.5]non-1-en-1-yl)amino]-3-[4-
- ([2,7]naphthyridin-1-ylamino)phenyl]propanoic acid
- (2S)-2-[(2-Isopropylsulfanyl-3-oxo-7-oxa-spiro[3.5]non-1-en-1-yl)amino]-3-[4-
- ([2,7]naphthyridin-1-ylamino)phenyl]propanoic acid
- (2S)-2-[(2-Bromo-3-oxo-spiro[3.4]octa-1,6-dien-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S) 2 [(4,4-Dimethyl-3-oxo-2-pentafluor ophenyl sulfanyl-cyclobut-1-enyl) amino] 3 (2S) 2 [(4,4-Dimethyl-3-oxo-2-pentafluor ophenyl sulfanyl-cyclobut-1-enyl) amino] 3 (2S) 2 [(4,4-Dimethyl-3-oxo-2-pentafluor ophenyl sulfanyl-cyclobut-1-enyl) amino] 3 (2S) (2S)
- {4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(4,4-Dimethyl-3-oxo-2-pyrazin-2-yl-cyclobut-1-enyl)amino]-
- 3-{4[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(7-Acetyl-2-bromo-3-oxo-7-aza-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-{[2-(Isopropylsulfanyl)-3-oxo-7-oxaspiro[3.5]non-1-en-yl)]amino}-3-(2,6-dimethoxy[1,1'-biphenyl]-4-yl)propanoic acid
- (2S)-2-[(2-Cyclohexyl-3-oxo-spiro[3.5]non-1-en-1-yl)amino]-3- $\{4$ -[(3,5-dichloroisonicotinoyl)amino]phenyl $\}$ propanoic acid
- (2S)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(2-methyl-3-oxo-
- spiro[3.5]non-1-en-1-ylamino)propanoic acid
- (2S)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(3-oxo-2-propyl-spiro[3.5]non-1-en-1-ylamino)propanoic acid

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(2S)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(2-methyl-3-oxo-7-oxa-spiro[3.5]non-1-en-1-ylamino)propanoic acid

(2S)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(3-oxo-2-propyl-7-oxa-spiro[3.5]non-1-en-1-ylamino)propanoic acid

(2S)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(2-[1,3]dithian-2-yl-3-oxo-spiro[3.5]non-1-en-1-ylamino)propanoic acid

(2S)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(2-ethyl-3-oxospiro[3.5]non-1-en-1-ylamino)propanoic acid

(2S)-3-{4-[(3,5-Dichloro-1-oxy-pyridine-4-carbonyl)amino]phenyl}-2-(3-oxo-spiro[3.5]non-1-en-1-ylamino)propanoic acid

(2S)-2-(2-Bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloro-1-oxy-pyridine-4-carbonyl)amino]phenyl}propanoic acid

(2S)-2-(2-Chloro-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloro-1-oxy-pyridine-4-carbonyl)amino]phenyl}propanoic acid

(2S)-3-{4-[(3,5-Dichloro-1-oxy-pyridine-4-carbonyl)-amino]-phenyl}-2-(2-methanesulfinyl-4,4-dimethyl-3-oxo-cyclobut-1-enylamino)

propanoic acid

(2S)-2-(2-Bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-[4-(3-methyl-[2,7]naphthyridin-1-ylamino)phenyl]propanoic acid

(2S)-2-(2-Bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-[4-

([2,7]naphthyridin-1-ylamino)phenyl]propanoic acid

(2S)-2-(2-Bromo-4,4-dimethyl-3-oxo-cyclobut-1-enylamino)-3-[4-(3-methyl-2,7]naphthyridin-1-yloxy)phenyl]propanoic acid

(2S)-2-[(2-Bromo-3-oxo-spiro[3.4]oct-1-en-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid and the salts, solvates, hydrates, N-oxides and carboxylic acid esters thereof.

23. (Original) A compound which is:

(2S)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid

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 $(2S)-2-[(2-Bromo-3-oxo-7-oxaspiro[3.5]non-1-en-1-y])amino]-3-{4-[(3,5$ dichloroisonicotinoyl)amino]phenyl}propanoic acid  $(2S)-2-[(2-Bromo-3-oxospiro[3.6]dec-1-en-1-yl)amino]-3-{4-[(3,5-1)]}$ dichloroisonicotinoyl)amino]phenyl}propanoic acid  $(2S)-2-\{(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-\{4-[(3-6)]amino\}-3-[(3-6)]amino\}-3-[(3-6)]amino]amino\}-3-[(3-6)]amino$ methyl[2,7]naphthyridin-1-yl)oxy]phenyl}propanoic acid (2S)-2-{[2-(Phenylsulfanyl)-4,4-dimethyl-3-oxo-1-cyclobutenyl]amino}-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid (2S)-2-[(2-Chloro-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5dichloroisonicotinoyl)amino]phenyl}propanoic acid (2S)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(3-oxo-2-pyridin-3yl-spiro[3.5]non-1-en-1-ylamino)propanoic acid (2S)-2-[(2-Iodo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5dichloroisonicotinoyl)amino]phenyl}propanoic acid (2S)-2-[(2-Bromo-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{5-[(3,5dichloroisonicotinoyl)amino]pyridin-2-yl}propanoic acid (2S)-2-[(2-Chloro-3-oxospiro[3.5]non-1-en-1-yl)amino]-3-{5-[(3,5dichloroisonicotinoyl)amino]pyridin-2-yl}propanoic acid (2S)-2-[(2-Chloro-3-oxo-7-oxa-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5dichloroisonicotinoyl)amino]phenyl}propanoic acid (2S)-2-[(2-Chloro-3-oxo-spiro[3.6]dec-1-en-1-yl)amino]-3-{4-[(3,5dichloroisonicotinoyl)amino]phenyl}propanoic acid (2S)-2-[(2-Bromo-3,7,7-trioxo-7 $\Box$ <sup>6</sup>-thia-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5dichloroisonicotinoyl)amino|phenyl}propanoic acid (2S)-2-[(2-Chloro-3-oxo-spiro[3.4]oct-1-en-1-yl)amino]-3-{4-[(3,5dichloroisonicotinoyl)amino]phenyl}propanoic acid (2S)-2-[(2-Bromo-3-oxo-spiro[3.4]oct-1-en-1-yl)amino]-3-{4-[(3,5dichloroisonicotinoyl)amino]phenyl}propanoic acid (2S)-2-[(2-Methylsulfanyl-3-oxo-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-

dichloroisonicotinoyl)amino|phenyl}propanoic acid

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- (2S)-2-(2-Fluoro-3-oxo-spiro[3.5]non-1-en-1-ylamino)3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(2-Fluoro-3-oxo-7-oxa-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(4,4-Dimethyl-2-methylsulfanyl-3-oxo-cyclobut-1-enyl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(2-Isopropylsulfanyl-4,4-dimethyl-3-oxo-cyclobut-1-enyl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(2-Isopropylsulfanyl-3-oxo-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(2-Isopropylsulfanyl-4,4-dimethyl-3-oxo-cyclobut-1-enyl)amino]-3-[4-
- ([2,7]naphthyridin-1-ylamino)phenyl]propanoic acid
- (2S)-2-[(2-Isopropylsulfanyl-3-oxo-spiro[3.5]non-1-en-1-yl)amino]-3-[4-
- ([2,7]naphthyridin-1-ylamino)phenyl]propanoic acid
- (2S)-2-[(2-Isopropylsulfanyl-3-oxo-7-oxa-spiro[3.5]non-1-en-1-yl)amino]-3-[4-
- ([2,7]naphthyridin-1-ylamino)phenyl]propanoic acid
- (2S)-2-[(2-Bromo-3-oxo-spiro[3.4]octa-1,6-dien-1-yl)amino]-3-{4-[(3,5-dienloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(7-Acetyl-2-bromo-3-oxo-7-aza-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)-2-[(2-Cyclohexyl-3-oxo-spiro[3.5]non-1-en-1-yl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid
- (2S)3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(2-methyl-3-oxospiro[3.5]non-1-en-1-ylamino)propanoic acid
- (2S)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(3-oxo-2-propyl-spiro[3.5]non-1-en-1-ylamino)propanoic acid
- (2S)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-2-(2-[1,3]dithian-2-yl-3-oxo-spiro[3.5]non-1-en-1-ylamino)propanoic acid
- (2S)-2-(2-Bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloro-1-oxy-pyridine-4-carbonyl)amino]phenyl}propanoic acid

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2-(2-Chloro-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloro-1-oxy-pyridine-4-carbonyl)amino]phenyl} propanoic acid and the salts, solvates, hydrates, N-oxides and carboxylic acid esters thereof.

## 24. (Original) A compound which is:

Ethyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

Isopropyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

t-Butyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

1-Methyl-piperidin-4-yl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

Phenyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

Cyclopentyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-

 $[(3,5\text{-}dichloroisonicotinoyl) a mino] phenyl\} propano ate$ 

2-Imidazol-1-yl-ethyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

Neopentyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

Tetrahydro-furan-3-yl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

Pyridin-4-ylmethyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl} propanoate

Tetrahydropyran-4-yl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

5-Methyl-2-oxo-[1,3]dioxol-4-ylmethyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-[(3,5-dichloroisonicotinoyl)amino]-phenyl}propanoate

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1-Methyl-pyrrolidin-3-yl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-

{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

2,3-Dihydroxypropyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-{4-

[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

Tetrahydrofuran-2-ylmethyl (2S)-2-(2-bromo-3-oxo-spiro[3.5]non-1-en-1-ylamino)-3-

{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoate

and the salts, solvates, hydrates and N-oxides thereof.

25. (Original) A pharmaceutical composition comprising a compound according to

claim 1 together with one or more pharmaceutically acceptable carriers, excipients or

diluents.

26. (Original) A method for the prophylaxis or treatment of a disease or disorder in a

mammal in which the extravasation of leukocytes plays a role, comprising

administering to a mammal suffering from such a disease or disorder a therapeutically

effective amount of a compound according to claim 1.

27. (Original) A method according to claim 26 wherein said disease or disorder is

selected from the group consisting of inflammatory arthritis, multiple sclerosis,

allograft rejection, diabetes, inflammatory dermatoses, asthma and inflammatory

bowel disease.

28. (Original) A method according to claim 27 wherein said inflammatory arthritis is

selected from the group consisting of rheumatoid arthritis vasculitis and

polydermatomyositis.

29. (Original) A method according to claim 27 wherein said inflammatory dermatoses

are selected from the group consisiting of psoriasis and dermatitis.

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30. (Original) A method for inhibiting, in a mammal, the binding of a4 integrins to the ligands thereof, comprising administering to the mammal an effective amount of a compound according to claim 1.

31. A method according to claim 30 wherein said  $\alpha 4$  integrins are selected from the group consisiting of  $\alpha 4\beta 1$  and  $\alpha 4\beta 7$  integrins.